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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/547,842	05/15/2006	Lorenzo A Pinna	2503-1169	9682

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ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/547,842	PINNA ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-20 remain in the case.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, the acronym "ALK" should not be used until fully defined at its first occurrence in the independent claim, such as by --anaplastic lymphoma kinase (ALK)--. In these claims, --SEQ ID NO: -- should be recited so as not to prematurely terminate the claim with an inappropriate period. Method claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim. In these claims the metes and bounds of the invention for which applicant desires coverage are not clear because it is not clear if the peptide comprises or consists of the recited sequence alternatives.

In claims 2-14, --The-- method should be recited for proper reference to the previously recited claim components.

In claim 5 and claims dependent thereupon, "the" entire catalytic domain lacks antecedent basis and its structure is not clear in the absence of recitation of the relevant SEQ ID NO: identifier to identify the relevant residues.

Claim 6 and claims dependent thereupon are not clear in the recitation of "Leulo to Alla'", it is believed --a fragment consisting of residues Leu^{1073} to Ala^{1459} of the ALK protein (SEQ ID NO: 5)-- was intended.

In claim 7 and claims dependent thereupon, "the" amount lacks antecedent basis.

Claim 10 is indefinite because without any additional active, positive steps delimiting how the method is actually practiced it is unclear what method/process applicant is intending to encompass beyond that set forth in claim 1. In this claim, "the" identification lacks antecedent basis.

In claim 11, the interrelationships of the newly recited steps to the previously recited steps are not clear, e.g. it is not clear if these steps are performed in parallel with, or substituted for, the steps of claim 1.

In claim 12, recitations of "the" candidate compound lacks antecedent basis in claim 10, it is believed claim --11-- was intended. In this claim, "the" same conditions also lack antecedent basis.

Claim 14 and claims dependent thereupon are entirely vague because no formula "(I)" is presented. Limitations from the specification are not imported unnecessarily into the claims. Further, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim

indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, the claim recites the broad recitation "halogen", and the claim also recites "preferably chlorine" which is the narrower statement of the range/limitation.

In claim 15 and claims dependent thereupon, --SEQ ID NO: -- should be recited so as not to prematurely terminate the claim with an inappropriate period. In these claims the metes and bounds of the invention for which applicant desires coverage are not clear because it is not clear if the peptide comprises or consists of the recited sequence alternatives.

In claim 16, --The-- peptide should be recited for proper reference to the previously recited claim components.

Claim 17 provides for the use of a peptide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. A method claim should also clearly state each component used in the method and the relationship of the various components. A method claim should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim. In this claim, --the-- peptide should be recited for proper reference to the previously recited claim components. In this claim, "the" determination lacks antecedent basis.

Claim 18 provides for the use of a compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. A method claim should also clearly state each component used in the method and the relationship of the various components. A method claim should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim. In this claim, --the-- compound should be recited for proper reference to the previously recited claim components. In this claim, "the" preparation or treatment lack antecedent basis. Further, a broad range or limitation (e.g. ALK-related tumors) together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) (e.g. especially anaplastic large cell lymphoma and non-Hodgkin lymphoma) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Moreover, improper Markush language is used to claim the members of the group. The alternatives "or" or "selected from the group consisting of...and" are acceptable.

In claim 19 and claims dependent thereupon, --SEQ ID NO: -- should be recited so as not to prematurely terminate the claim with an inappropriate period. In these claims the metes and bounds of the invention for which applicant desires coverage are not clear because it is not clear if the peptide comprises or consists of the recited sequence alternatives.

In claim 20, --The-- kit should be recited for proper reference to the previously recited claim components. It is not clear what applicant intends as encompassed by "reagents for colorimetric reactions."

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17 and 18 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, 10, 15, 17, 19, and 20 are rejected under 35 U.S.C. § 102(b) as being anticipated by Morris et al. (US 5,770,421) in light of Hanks et al. (Science 241: 42, 1988).

Morris et al. provided anaplastic lymphoma kinase (ALK) (SEQ ID NO: 2, Fig. 3) or a fusion protein comprising a catalytic domain thereof (SEQ ID NO: 4) and determined autophosphorylation of the proteins (see e.g. cols. 36-37, and Figs. 12-13), which comprise SEQ ID NO: 2 of the instant application (residues 1274-1294 of SEQ ID NO: 5 of the instant application and SEQ ID NO: 2 of the reference; residues within SEQ ID NO: 15 of the

reference). In light of Hanks et al., autophosphorylation of the catalytic domains of protein kinases occurs within 20 residues upstream of a conserved triplet (which can be PPE in tyrosine kinases) in subdomain VIII of the catalytic domain (see page 45, col. 2, and page 48) which is found at residues 1297-1299 of the ALK sequence of Morris et al. (SEQ ID NO: 5 of the instant application and SEQ ID NO: 2 of the reference), thus the phosphotyrosine residues determined by Morris et al. were inherently within residues 1277-1296 of ALK.

Claims 1, 3-5, 10-12, 15, 17, 19, and 20 are rejected under 35 U.S.C. § 102(b) as being anticipated by Turturro et al. (Clin. Can. Res. 8: 240, 2002) in light of Morris et al. (US 5,770,421) and Hanks et al. (Science 241: 42, 1988).

Turturro et al. determined the effects of protein kinase inhibitors on the autophosphorylation of the anaplastic lymphoma kinase (ALK) catalytic domain to screen for therapeutic compounds. In light of Hanks et al., autophosphorylation of the catalytic domains of protein kinases occurs within 20 residues upstream of a conserved triplet (which can be PPE in tyrosine kinases) in subdomain VIII of the catalytic domain (see page 45, col. 2, and page 48) which is found at residues 1297-1299 of the ALK sequence in light of Morris et al. (SEQ ID NO: 5 of the instant application and SEQ ID NO: 2 of Morris et al.), thus the phosphotyrosine residues determined by Turturro et al. were inherently within residues 1277-1296 of ALK.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1, 3-12, 15, and 17-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Turturro et al. (Clin. Can. Res. 8: 240, 2002), Morris et al. (US 5,770,421), Hanks et al. (Science 241: 42, 1988), Hirth et al. (US 5,763,198), Strulovici (US 5,759,787), and Schraag et al. (Anal. Biochem. 211: 233, 1993).

The teachings of Turturro et al., in view of the teachings of Hanks et al. and Morris et al., are essentially as set forth above and differ from the invention as instantly claimed in not teaching detection of phosphotyrosine in the autophosphorylation reaction of ALK with antibodies in immunoassays or with substrates consisting of smaller peptides.

Hirth et al. teach methods for screening compounds for their effects on the ability of tyrosine kinases to autophosphorylate or phosphorylate a substrate of interest using target cells or cell-free systems (see in particular: col. 6, lines 15-40; col. 13; cols. 16-17). Substrate is bound to a solid support and the phosphorylation state of the substrate is determined with an anti-phosphotyrosine antibody, which can be labeled directly or indirectly with a secondary reagent such as a labeled anti-immunoglobulin (see e.g. section 5.5 bridging cols. 11-12). The substrate can be bound to a solid support by an anti-substrate antibody.

Strulovici also teaches methods for screening compounds for their modulatory effects on kinase activity using tags on the substrate and receptors therefor, such as antibodies (see e.g. cols. 2-3). The reference teaches that the substrates can be peptides derived from targets of the kinase being assayed (see e.g. cols. 5-6) containing the kinase recognition motif (see e.g. col. 1). The reference teaches the method as an alternative to prior assays that used incorporation of radioactive phosphate.

Schraag et al. teach methods for the detection of tyrosine kinase activity using substrate immobilized by adsorption, incubation with kinase, and detection with anti-phosphotyrosine antibodies and labeled anti-immunoglobulin antibodies, essentially the method as instantly disclosed and claimed but differing therefrom by not specifically teaching ALK as the kinase or peptides derived therefrom as the substrate. The method is taught as a simple, nonlaborious alternative to existing methods using radiolabeled adenosine triphosphate.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted antibodies and immunoassay methods for the determination of autophosphorylation of anaplastic lymphoma kinase (ALK) in Turturro et al. for the determination of the effects of protein kinase inhibitors on the autophosphorylation of the ALK catalytic domain to screen for therapeutic compounds because such techniques were well known in the art as taught by Hirth et al., Strulovici, and Schraag et al. motivated by the simple, nonlaborious and non-radioactive nature of these alternatives to the radio-labeled phosphate incorporation method used by Turturro et al. It would have been further obvious to one of ordinary skill in the art to have substituted any peptide comprising tyrosine residues within residues 1277-1296 of the ALK sequence taught by Morris et al. in the assays of Turturro et al.,

as modified above by Hirth et al., Strulovici, and Schraag et al., because one would have reasonably expected the autophosphorylation site of ALK to reside in this region in view of the combined teachings of Hanks et al. and Morris et al. and one would have been motivated to provide a peptide substrate containing the kinase recognition motif as is conventional in the art as taught in Strulovici. It would have been further obvious to one of ordinary skill in the art that ALK, or ALK peptides, comprising the autophosphorylation site could be immobilized prior to or after autophosphorylation with receptors, particularly antibodies or avidins, or prior to autophosphorylation by adsorption in the method of Turturro et al., as modified, in view of the conventional alternatives of substrate immobilization taught in Hirth et al., Strulovici, and Schraag et al. for such assays.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Epstein et al. (US 5,599,681) teach activation state specific phosphoprotein antibodies.

Angeles et al. (Anal. Biochem. 236: 49, 1996) teach immobilization of a physiologically relevant substrate for detection of kinase activity by enzyme-linked immunosorbent assay.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
April 16, 2009

/Ann Y. Lam/
Primary Examiner, Art Unit 1641
March 21, 2009